Remarks

Claims 1, 3, 6-9, 11, 12, 15, 18, 19, 43, 45-50, 52-58, 60, 62, 64, 66, and 68-73 were pending in the subject application. By this Amendment, claims 1, 18, 19, 43, 49, 52, 58, 60, 62, 64, and 66 have been amended, claims 11, 54-57, and 68-70 have been cancelled, and new claims 74 and 75 have been added. The undersigned avers that no new matter is introduced by this amendment. Entry and consideration of the amendments presented herein is respectfully requested. It should be understood that the amendments presented herein have been made solely to expedite prosecution of the subject application to completion and should not be construed as an indication of the applicants' agreement with or acquiescence in the Examiner's position. Accordingly, claims 1, 3, 6-9, 12, 15, 18, 19, 43, 45-50, 52, 53, 58, 60, 62, 64, 66, and 71-75 are currently before the Examiner for consideration. Favorable consideration of the pending claims is respectfully requested.

Submitted herewith is a Request for Continued Examination (RCE) under 37 C.F.R. §1.114, including a request for suspension of action, for the subject application.

Claims 54-57, 69, and 70 have been rejected under 35 U.S.C. §103(a) as being obvious over Hogan *et al.* (*Eur. J. Immunol.*, 1998, 28:413-423), in view of Li *et al.* (*J. Immunol.*, 1996, 157:3216-3219), Dow *et al.* (U.S. Patent No. 6,693,086), and O'Donnell *et al.* (*J. Immunol.*, 1999, 163:4246-4252). The applicants respectfully submit that the claimed invention is not obvious in view of the cited references. However, by this Amendment, the applicants have cancelled claims 54-57, 69, and 70, rendering this rejection moot. Accordingly, withdrawal of the rejection under 35 U.S.C. §103(a) is respectfully requested.

Claims 1, 3, 6-9, 11, 12, 15, 18, 19, 43, 45-50, 52-58, 60, 62, 64, 66, and 68-73 have been rejected under 35 U.S.C. §112, first paragraph, as non-enabled by the subject specification. The applicants respectfully submit that the claimed invention is fully enabled by the specification.

By this Amendment, independent claims 1 and 43 have been amended to recite "such that the co-administering results in an increase of IFN-γ and IL-2 production, an increase of IgG2a specific to the antigen, a decrease of IL-4 production, and reduced serum IgE." At page 7, the Office Action acknowledges that the application provides enablement for "an increase of Th1-type cytokines IFN-γ and IL-2, an increase in the levels of IgG2a specific to said antigen, a decrease of the Th2-type

cytokine IL-2, and reduced serum IgE levels". Where the Office Action recites "a decrease of the Th2-type cytokine IL-2", the applicants presume that "a decrease of Th2-type cytokine IL-4" was intended. As acknowledged at page 11, lines 11-12, of the Office Action, these cytokine profiles are demonstrated in the specification (*e.g.*, Examples 1-5). Claims 1 and 43 have also been amended to recite that the nucleic acid sequences are administered to a mammal. Support for this amendment can be found, for example, at page 5, lines 17-21; and page 11, lines 21-29, of the specification.

In addition to intramuscular administration and subcutaneous injection, the specification teaches other forms of administration. For example, page 12, third paragraph, of the specification incorporates U.S. Patent No. 6,489,306 by reference, which describes an example of intranasal administration that may be utilized to administer the nucleic acid sequences claimed in this application. Thus, the applicants need not describe every administration route. Nevertheless, many references describe successful administration routes in immunology. Roy, in U.S. Patent No. 6,475,995, on column 2, lines 46-49, has noted that *successful immunization* has been demonstrated with administration of plasmid DNA by *intramuscular, intradermal, intravenous and subcutaneous* routes. Wahren and Lu, in their review article, *DNA Vaccines: An Overview*, page 4, last paragraph, have noted that DNA vaccines have been delivered by a variety of routes. Felgner, in U.S. Patent No. 6,710,035, describes many routes of administering plasmids encoding immunogenic peptides which include *intramuscular, intravenous, intranasal, subcutaneous, and intradermal* routes (column 23, line 60 to column 24, lines 1-4; Examples 15-18; and claims 12-17, for example). Thus, a person of ordinary skill in the art would be able to use well-known successfully used gene delivery routes for immunotherapy. The initial burden is on the Examiner to establish a reasonable basis for questioning the enablement of the invention. A patent specification need not set forth clear and convincing evidence "proving" its conclusions. Rather, the applicants' statements and assertions are to be taken as true, and rejected only if the underlying facts are found to be untruthful or inaccurate, *i.e.*, only if the asserted claim is "incredible" or "impossible". *In re Marzocchi*, 169 USPQ 367, 370 (CCPA 1971). Furthermore, even if the immune response would not be modulated using every potential route of co-administration, in all mammals, it is well established that the presence of inoperative embodiments within the scope of a claim does not necessarily render a claim non-enabled (MPEP 2164.08(b)).

At page 11, the Office Action indicates that the claims encompass "any sequence encoding said amino acids, including fragments thereof" and amino acid sequences that do not have the biological activity of IL-12 and IFN-γ. Independent claims 1 and 43 recite:

"a nucleic acid sequence encoding p35 and p40 subunits of human IL-12, and a promoter sequence operably linked to the nucleic acid sequence encoding the p35 and p40 subunits"; and

"a nucleic acid sequence encoding human IFN-γ, and a promoter sequence operably linked to the nucleic acid sequence encoding human IFN-γ".

Thus, claims 1 and 43 require that the nucleic acid sequences encode the p35 and p40 subunits of human IL-12, and human IFN-γ. The dependent claims incorporate all the limitations of independent claims 1 or 43. Fragments of the p35 and p40 subunits of IL-12, or of IFN-γ, are not recited in the claims.

The applicants respectfully submit that the claims as currently amended are commensurate in scope with the enablement of the subject specification. Accordingly, reconsideration and withdrawal of the rejection under 35 U.S.C. §112, first paragraph, is respectfully requested.

In view of the foregoing remarks and amendments to the claims, the applicants believe that the currently pending claims are in condition for allowance, and such action is respectfully requested.

The Commissioner is hereby authorized to charge any fees under 37 C.F.R. §§1.16 or 1.17 as required by this paper to Deposit Account 19-0065.

The applicants invite the Examiner to call the undersigned if clarification is needed on any of this response, or if the Examiner believes a telephonic interview would expedite the prosecution of the subject application to completion.

Respectfully submitted,

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